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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/576,097	05/22/2000	Laman Alani	6499.US.O2	3170

23492 7590 08/09/2002

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EXAMINER
LUKTON, DAVID

ART UNIT	PAPER NUMBER
1653	12

DATE MAILED: 08/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/576,097	ALANI ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *21 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-11 and 14-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-11 and 14-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Pursuant to the directives of paper No. 10 (filed 5/21/02), claims 2, 12, 13 have been cancelled, claims 1, 3-6, 10, 11, 14, 15, 17, 18 amended, and claims 20-21 added. Claims 1, 3-11, 14-21 are pending.

Applicants' arguments filed 5/21/02 have been considered and found persuasive in part.

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The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-11, 14-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims recite the term "pharmaceutical composition", which implies an assertion of therapeutic efficacy. However, no such efficacy is in evidence. Applicants have argued that ritonavir is effective to inhibit HIV protease. Applicants have also argued that there exists a single person, or perhaps a group of persons, who have "approved" ritonavir and who believe that ritonavir is both safe and efficacious. However, the single person, or group of persons to which applicants have referred has not been identified. Accordingly,

the single person, or group of persons in question may or may not be qualified to make such a judgement. Nevertheless, the examiner will stipulate that (a) ritonavir will inhibit HIV replication, both *in vitro* and *in vivo*, and (b) when adminstered to humans, there exists a dosage sufficiently high that HIV replication is inhibited, but which at the same time, does not induce a life-threatening illness. However, this is not the same as therapeutic efficacy. A therapeutically effective drug is one which will provide a perceptible improvement in the condition of a patient who is afflicted with AIDS, and is exhibiting clear signs of immunosuppression. However, there is no evidence that this is the case. As a first step in the dialog, it is suggested that applicants provide some evidence that ritonavir is effective to treat AIDS patients, especially when given in the absence of other antiviral drugs. The claims encompass compositions which contain no active agents other than ritonavir; accordingly, even if it were true (and it is not) that a reference were to disclose that a particular combination of ritonavir and another agent "X" could completely cure 100% of all AIDS patients, such a reference would not provide the basis for a finding of enablement of the claimed invention.

Secondly, the claims mandate the presence of other ingredients which will alter the bioavailability of the ritonavir. No doubt applicants believe that such other ingredients provide a more efficacious composition. However, there is no evidence either for or against such a proposition. Accordingly, it is entirely possible that the bioavailability of

the claimed compositions is substantially lower than those which have been previously administered to humans. Thus, applicants are beginning with a compound which may not be therapeutically effective to begin with, and subsequently adding other compounds which may cause a substantial decrease in whatever efficacy the ritonavir may exhibit to begin with. If applicants do not have evidence of therapeutic efficacy, it is suggested that the term "pharmaceutical" be eliminated from the claims.

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Claims 1, 3-11, 14-21 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- In claim 1, the phrase "the total solution" occurs several times. In each case, this term lacks antecedent basis. A related issue is that if one has oleic acid and water in a weight ratio which exceeds 10, the result is not going to be a solution at all; oleic acid is not soluble in water, and does not form a solution with water. Moreover, the situation is not helped when significant a amount of ritonavir is present. For example, if the mixture were to consist of 75% oleic acid, 5% propylene glycol, 19% ritonavir, and 1% H_2O, exactly how would applicants propose to obtain a liquid in which all components are fully dissolved? (see also claims 14, 15 and 20).

- In claim 10, the last compound listed is the following: (parentheses and numbers eliminated for simplicity):

  dimethylethylaminocarbonyl-methylpropylamino-hydroxy-phenylmethylpropyl-quinolinylcarbonylaminobutanediamide.

  In this compound name, there is a total of seven left hand square brackets ("[") and only five right hand square brackets ("]"). In addition, between the number "2"

and the term "quinolinylcarbonyl", there should be a hyphen.

- In the claims, the terms "ritonavir", "indinavir", "saquinavir", "nelfinavir" and "tipranavir" may be used if accompanied by the chemical name (or structure) that these terms represent.

- Most of the claims recite the term "about" in reference to a range. For example, claim 1, part (a) recites the following: "about 1% to about 50%". The presence of the term "about" renders the claims indefinite as to the upper and lower limits. It is suggested that the term "about" be deleted when it refers to a range.

- Claim 1 recites weight percentages. At the lower end, the claim permits the ritonavir, solvent and water to constitute only 42.4% of the total mixture. For this embodiment, the claim mandates the presence of at least one other component that constitutes 57.6% of the total composition. Thus, the claim mandates that more than half of the claimed composition consists of a "mystery component". The claim is thus rendered indefinite is the "mystery component" a carrier, is it gelatin, is it another drug? If there is an adequate written description, applicants can overcome this ground of rejection without necessarily limiting scope. For example, if there is a written description for it, the claims could be amended to simply recite that a carrier must be present in an amount such that the various recited ingredients add up to 100%. At the other end of the spectrum, claim 1 permits the ritonavir, solvent and water to constitute 143% of the total, even before adding a surfactant in any amount. Thus, what does it mean, physically, when the ingredients add up to 143% or 150% of the total composition? This ground of rejection applies to all of the other claims as well.

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The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1, 3-11, 14-21 are rejected under 35 U.S.C. §103 as being unpatentable over Sham (WO 97/21685) in view of Yamamoto (USP 5,264,223) or Yamamoto (USP 5,756,123).

Sham discloses (beginning on page 126, last paragraph) the invention substantially as claimed, except for the presence of water. Yamamoto ('223) discloses capsules in which the water content is about 5%; Yamamoto ('123) discloses capsules in which the water content is in the range of 1-6%. Yamamoto does not disclose the claimed compositions.

In the instant claims, it is recited that the quantity of water which is in the range of 0.4% to 3.5%. However, despite the presence of the phrase "by weight of the total solution", there is no requirement that a solution, if even required by the claim, contains water. The claims encompass the possibility of a completely anhydrous composition being contained within a capsule that contains a small quantity of water such that the overall composition, including the capsule, contains 0.4% to 3.5% water. It is to this embodiment that the rejection is targetted.

Suppose, for example, that one took 300 mg of a mixture, exclusive of the capsule,

containing ritonavir, oleic acid and ethanol (as disclosed in Sham, page 127) and placed it in a capsule weighing 100 mg *as per* Yamamoto. In such a case, the overall composition would contain about 195 mg oleic acid, 20 mg ethanol, and 5 mg water. Given that the total weight of the composition would then be 400 mg, the weight percent of oleic acid, ethanol, and water would then be 48%, 5% and 1.25%, respectively, thereby meeting the requirements of the claims.

Thus, the claims are rendered obvious.

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Claims 1, 3-11, 14-21 are rejected under 35 U.S.C. §103 as being unpatentable over Al Razzak (USP 5948436).

As indicated previously, Al Razzak teaches the elements of the claimed invention. Applicants have argued that the compositions of Al Razzak do not contain fatty acids. It may be true that the disclosed compositions do not contain free fatty acids, but they contain fatty acids nontheless, as indicated in col 6, line 50+.

Thus, the claims are rendered obvious.

*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton. Phone: (703) 308-3213.

An inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

DAVID LUKTON
PATENT EXAMINER
GROUP 1800